STN Search History

FILE 'HOME' ENTERED AT 12:12:59 ON 11 FEB 2004

L1 577 (SAQUINAVIR OR AMPRENAVIR OR INDINAVIR OR NELFINAVIR OR RITONAVI R OR PROTEASE (A) INHIBITOR) (S) (IMMUNOASSAY OR EIA OR ELISA OR SANDWICH (A) ASSAY)

L5 265 L1 AND (ANTIBOD#### OR BIND### OR LIGAND OR RECEPTOR) (S) (SAQUI NAVIR OR AMPRENAVIR OR INDINAVIR OR NELFINAVIR OR PROTEASE (A) INHIBITOR)

(FILE 'HOME' ENTERED AT 12:12:59 ON 11 FEB 2004)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 12:13:35 ON 11 FEB 2004

L1 577 S (SAQUINAVIR OR AMPRENAVIR OR INDINAVIR OR NELFINAVIR OR RITON
L2 71 S L1 AND (HIV## OR AIDS)
L3 0 S L1 AND PY<200
L4 396 S L1 AND PY<2000
L5 265 S L1 AND (ANTIBOD#### OR BIND### OR LIGAND OR RECEPTOR) (S) (SA
L6 191 S L4 AND L5
L7 114 DUP REM L6 (77 DUPLICATES REMOVED)
L8 21 S L7 AND SANDWICH
L9 38 DUP REM L2 (33 DUPLICATES REMOVED)
L10 38 S L9 NOT L8
L11 17 S L10 AND ANTIBOD#####
L12 17 S L10 AND L4
L13 8 S L11 AND L12
L14 449 S L1 AND PY<2001
L15 22 S L10 AND L14

L15 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:22245 CAPLUS
DN 124:115491
TI A simple **immunoassay** to detect **protease inhibitors** in microbial fermentation broths
AU Carrano, Lucia; Guindani, Ambra; Denaro, Maurizio; Islam, Khalid
CS Lepetit Res. Cent., Marion Merrell Dow Res. Inst., Gerenzano, 21040, Italy
SO Journal of Antibiotics (**1995**), 48(12), 1511-14
CODEN: JANTAJ; ISSN: 0021-8820
PB Japan Antibiotics Research Association
DT Journal
LA English
AB A simple assay is described that uses a single substrate and a single detection system for proteolytic enzymes belonging to different classes. Tubulin, the microtubule subunit protein, and a com. available monoclonal antibody that recognizes the C-terminal tyrosine residue were used in an assay to detect inhibitors of different classes of proteases and also provide information on the specificity and potency of the mol.

L15 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:51743 CAPLUS
DN 118:51743
TI An ultrasensitive human immunodeficiency virus type 1 protease radioimmuno rate assay with a potential for monitoring blood levels of protease inhibitors in acquired immunodeficiency disease syndrome patients
AU Evans, David B.; Vosters, Anne F.; McQuade, Thomas J.; Sharma, Satish K.
CS Upjohn Co., Kalamazoo, MI, 49001, USA
SO Analytical Biochemistry (**1992**), 206(2), 288-92
CODEN: ANBCA2; ISSN: 0003-2697
DT Journal
LA English
AB The angiotensin I-based peptide Asp-Arg-Val-Tyr-He-His-Pro-Phe-His-Leu-Leu-Glu-Glu-Ser yields angiotensin I (AngI) and Leu-Glu-Glu-Ser upon hydrolysis by the human immunodeficiency virus type 1 (**HIV**-1) protease, but not by human renin. N-terminal sequencing of the reaction products showed that the **HIV**-1 protease cleaved exclusively at the Leu-Leu bond. The rate of Ang I formation can be measured by a RIA, since the parent peptide has minimal cross reactivity in this assay. The rate of enzymic hydrolysis is maximum at pH 4.5-5.0 and at an ionic strength of 1 M. At 37°C, 0.1 M Na acetate buffer, pH 5.0, 1 M NaCl, 10% glycerol, 5% ethylene glycol, 1 mg/mL bovine serum albumin, and 3 mM EDTA, the reaction obeys Michaelis-Menten type kinetics with Km = 17.2 μM and kcat = 2.30 min-1. The activity assay readily quantitates as little as 0.25 nM of **HIV**-1 protease. The production of Ang I by the **HIV**-1 protease is inhibited in the presence of a **HIV**-1 protease inhibitor. The newly discovered substrate is relatively insensitive to human or monkey serum. Therefore, the effect of sera from 20 patients with advanced acquired immunodeficiency disease syndrome (**AIDS**) on Ang I production in the above assay system was examined Results of this study indicate that it may be possible to adapt the above Ang I-based system to determine blood levels of **HIV**-1 protease inhibitors in **AIDS** patients during clin. trials.

L15 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:156511 CAPLUS
DN 114:156511
TI A high throughput assay for inhibitors of **HIV**-1 protease. Screening of microbial metabolites
AU Sarubbi, Edoardo; Nolli, M. Luisa; Andronico, Franca; Stella, Sergio;

Saddler, Gerard; Selva, Enrico; Siccardi, Antonio; Denaro, Maurizio
CS Lepetit Res. Cent., MMDRI, Gerenzano, 21040, Italy
SO FEBS Letters (**1991**), 279(2), 265-9
CODEN: FEBLAL; ISSN: 0014-5793
DT Journal
LA English
AB A novel method for discovery of **HIV**-1 protease inhibitors in complex biol. samples has been developed. The assay is based on 2 specific reagents: a recombinant protein constituted by a portion of the **HIV**-1 Gag polyprotein comprising the p17-p24 cleavage site, fused to Escherichia coli β-galactosidase, and a monoclonal antibody which binds the fusion protein in the Gag region. Binding occurs only if the fusion protein has not been cleaved by the **HIV**-1 protease. The assay has been adapted for the screening of large nos. of samples in standard 96-well microliter plates. Using this method about 12,000 microbial fermentation broths have been tested and several **HIV**-1 protease inhibitory activities have been detected. One of these has been studied in detail.

L15 ANSWER 17 OF 22 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
AN 95151800 EMBASE
DN 1995151800
TI Assay of **HIV**-1 protease activity by use of crude preparations of enzyme and biotinylated substrate.
AU Yu S.-L.; Wang N.; Liou C.-Y.; Syu W.-J.
CS Graduate Institute, Microbiology and Immunology, National Yang-Ming University, Shih-Pai 112,Taipei, Taiwan,Province of China
SO Journal of Virological Methods, (1995) 53/1 (63-73).
ISSN: 0166-0934 CODEN: JVMEDH
CY Netherlands
DT Journal; Article
FS 004 Microbiology
LA English
SL English
AB An enzyme **immunoassay** was developed for monitoring protease reactions of human immunodeficiency virus (**HIV**). The protease and its substrate, the gag precursor, were generated separately in Escherichia coli. The **HIV**-1 protease was generated with a glutathione-S-transferase expression system and the gag substrate, named Pin17/24, was prepared with a PinPoint expression system. Pin17/24 consists of an N-terminal peptide, which is biotinylated in E. coli, fused with a C-terminal peptide that contains a protease cleavage site flanked by p17 and p24 segments. Through its biotin in the N-terminal region, Pin17/24 bound to **ELISA** plates coated with avidin, whereas through its C-terminal region, the same molecule of Pin17/24 could be recognized by an anti-p24 monoclonal antibody. When the protease was added to Pin17/24, the p24 fragment was released from the biotinylated fusion protein and could no longer be retained on the avidin plates, and as a result, binding of the anti-p24 monoclonal antibody decreased. The binding was specific and the reaction was inhibited by a known **HIV** **protease inhibitor**. Due to the specific interactions between avidin and biotin, monoclonal antibody and antigen, and the **HIV** protease and the gag substrate, crude preparations of these reagents can be used readily in the assay. The simplicity and feasibility of this method should be useful for simultaneous monitoring of many enzyme reactions, particularly for screening possible **HIV** **protease inhibitors**

L15 ANSWER 19 OF 22 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN
AN 94329935 EMBASE
DN 1994329935
TI An HIV-1 protease screening assay using a non-infectious proviral clone.
AU Heldsinger A.A.; Antonucci T.
CS Schwarz Pharma, 5600 W County Line Road,Mequon, WI 53092, United States
SO Journal of Virological Methods, (1994) 49/3 (247-255).
ISSN: 0166-0934 CODEN: JVMEDH
CY Netherlands
DT Journal; Article
FS 004 Microbiology
037 Drug Literature Index
LA English
SL English
AB An in-vitro assay was developed to screen for **HIV**-1 **protease inhibitors** using a non-infectious proviral clone (X19) with a deletion in the envelope gene (Ratner et al., 1991). The proviral clone, X19, was expressed transiently in the COS 7 cell line. The virus was able to replicate as assessed by the presence of p24 in the supernatants, yet the virions produced did not infect CD4 positive cells. To determine the effect of a known **protease inhibitor** on p24 antigen production, PD 148310 (a Ro 31-8959 analog) was added immediately after transfection of the COS 7 cells: Virus particles were produced maximally after 24 h and cell supernatants were assayed for p24 antigen production using a p24 **ELISA** assay. PD 148310 inhibited p24 release in a dose-dependent manner with an IC50 of 23.6 nM. Western blot analysis of the supernatants using a mouse monoclonal antibody against p24 confirmed the presence of a well-defined p24 band in the control lane. At 1000 nM of PD 148310 the p24 band was not detectable, leaving only the unprocessed p55 Gag precursor. This technique is a useful tool to screen for potential **HIV**-1 **protease inhibitors**.

L15 ANSWER 20 OF 22 EMBASE
on STN
AN 93166332 EMBASE
DN 1993166332
TI Detection of inhibition of **HIV**-1 protease activity by an enzyme-linked immunosorbent assay (ELISA).
AU Mansfeld H.-W.; Schulz S.; Grutz G.; Von Baehr R.; Ansorge S.
CS Division of Experimental Immunology, Department of Internal Medicine, Medical Academy of Magdeburg, Leipziger Str. 44,3090 Magdeburg, Germany
SO Journal of Immunological Methods, (1993) 161/2 (151-155).
ISSN: 0022-1759 CODEN: JIMMBG
CY Netherlands
DT Journal; Article
FS 004 Microbiology
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LA English
SL English
AB An **ELISA** is described for the detection of **HIV**-1 protease activity using an immobilized gag-related polyprotein as substrate. Proteolyic activity was demonstrated with either bacterial lysates expressing **HIV**-1 protease or purified protease. No cleavage was observed with a protein preparation from control bacteria not expressing **HIV**-1 protease. Under these conditions the aspartyl-type **protease inhibitor**, pepstatin A, was found to inhibit **HIV**-1 protease cleavage by >90% at a concentration of 0.1 mM. This assay may be a useful tool for the study of

both synthetic and natural inhibitors of **HIV**-1 protease.

WEST Search History

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DATE: Wednesday, February 11, 2004

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=OR	
☐	L18	l17 and ligand with analyte same antibody with analyte	74
☐	L17	2000	145
☐	L16	L15 and sandwich	273
☐	L15	immunoassay same analyte same ligand same antibody	511
☐	L14	l11 and (analyte same ligand same antibody)	6
☐	L13	L12 and l11	44
☐	L12	L10 and sandwich same label with antibody	47
☐	L11	2000	416
☐	L10	(immunoassay same sandwich and antibody).ab.	468
☐	L8	l7 and l4	14
☐	L7	L6 not l5	252
☐	L6	antibod$3 with (bind$4 target$4 react$4 specif$6) with (protease adj inhibitor saquinavir amprenavir indinavir nelfinavir ritonavir)	268
☐	L5	L4 and l3	70
☐	L4	(saquinavir amprenavir indinavir nelfinavir ritonavir (HIV$2 with protease adj inhibitor)) with(immunoassay or ELISA or sandwich same assay or antibody)	175
☐	L3	L1 and (sandwich or ELISA)	135
☐	L2	L1 and sandwich or ELISA	44843
☐	L1	(saquinavir amprenavir indinavir nelfinavir ritonavir (HIV$2 with protease adj inhibitor)) same (immunoassay or ELISA or sandwich same assay or antibody)	367

END OF SEARCH HISTORY